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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	13

DATE MAILED: 01/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/382,837	Borodic, G.E.
Examiner	**Art Unit**
G. R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 5, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-19 and 21-23* is/are pending in the application.

4a) Of the above, claim(s) *9 and 13-16* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 10-12, 17-19, and 21-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Claims 1-8, 10-12, 17-19, and 21-23 are being acted upon.

2. The declaration is objected to because it claims priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846 as indicated in the first line of the specification. A new declaration is required.

In Paper No. 12, filed 11/05/01, Applicant has indicated that a new declaration will be submitted.

3. In view of Applicant's amendment and response, filed 11/05/01, only the following rejections remain.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2-4 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) in claim 2, the term "substantial" muscle weakness has not been defined, thus, the metes and bounds of the claim are indefinite. Note that in the instant context muscle weakness has not been defined, thus, said weakness might range from the undetectable to total paralysis. As such, "substantial" weakness is impossible to define,

B) in claim 4, "units" has not been defined, thus, the metes and bounds of the claim are indefinite. The specification discloses "units", "mouse units", and "LD 50 units", none of which are specifically defined in the specification, thus, the metes and bounds of the claim are indefinite, for the reasons of record as set forth in Paper No. 11, mailed 7/05/01.

Applicant's arguments, filed 11/05/01, have been fully considered but they are not persuasive. Applicant argues that "the term substantial muscle weakness would be clearly understood by one of ordinary skill in the medical arts". It is the Examiner's position that the actual metes and bounds of the term remain indefinite. Regarding the recitation of the term "units", Applicant argues that "These terms [units, mouse units or LD50 units] are used identically in the specification to refer to units of a chemodenervating pharmaceutical measured using the

mouse LD50 assay that is well-known by those of ordinary skill in the relevant art. However, the specification makes no such specific disclosure.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 17-23 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record as set forth in Paper No. 11, mailed 7/05/01. This is a new matter rejection.

Applicant's arguments, filed 11/05/01, have been fully considered but they are not persuasive. Applicant argues that the disclosure of "Chemodenervative pharmaceuticals such as botulinum toxin...are effective anti-inflammatory agents," or other passages relating to anti-inflammatory actions relating to nerve cells, "neural reflex mechanisms," or inflammation that "may be neurogenically mediated," is sufficient to support new claims drawn to neurogenic inflammation and neurogenic inflammatory mediators. It is the Examiner's position that the vague disclosure is insufficient to support the newly added specific claims.

Regarding Applicant's arguments that the specification provides sufficient support for claims drawn to methods of treating neurogenic inflammation by inhibiting specific inflammatory mediators, i.e., substance-P, calcitonin gene-related peptide, vasoactive intestinal peptide, interleukin-1, interleukin-2, nitric oxide, 5-hydroxytryptamine, tumor necrosis factor, and nerve growth factor, Applicant's arguments that "explicit references in the specification to "preformed mediators", "cytokines", and "newly-formed mediators" encompasses all of the specific neurogenic inflammatory mediators enumerated in claim 19," it is the Examiner's position that the specification is insufficient to support the specific claims. For example, a generic disclosure that cytokines might be involved in inflammatory mechanisms is insufficient to support new claims drawn to methods comprising a species of inhibiting a

specific cytokine involved in a specific type of inflammation.

Regarding Applicant's arguments that the specification provides sufficient support for claims drawn to methods of treating gout, it is the Examiner's position that the disclosure of the specification reciting the treatment of rheumatoid arthritis is insufficient to support claims drawn the treatment of gout, even though both conditions might be considered an inflammatory response in the joint as argued by Applicant.

Regarding Applicant's arguments that the specification provides sufficient support for claims drawn to methods of treating the neurogenic inflammation by inhibiting histamine, Applicant argues that the specification "explicitly states that "low dosages of the subject chemodenervative agent reduces histamine releases." However, it is the Examiner's position that the specification fails to adequately support said reduction in combination with the other limitations of Claims 17 and 23, e.g., the interruption of a neurogenic pathway associated with neurogenic inflammation.

8. Claims 2-5 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of reducing allergy induced conjunctivitis in a mouse by injecting 0.675 mouse units of botulinum toxin type A, does not reasonably provide enablement for:

A) a method of reducing inflammation without causing substantial muscle weakness,

B) a method of reducing inflammation comprising an effective dose of botulinum toxin less that 2.5 units,

C) a method of reducing inflammation comprising administering botulinum toxins B-G, for the reasons of record as set forth in Paper No. 11, mailed 7/05/01.

Applicant's arguments, filed 11/05/01, have been fully considered but they are not persuasive. Applicant argues that the single disclosed working example disclosing the treatment of conjunctivitis in a rat is sufficient to support the breadth of the claims; it is the Examiner's position that such is not the case, for the reasons of record, particularly in regards to the treatment of humans "without causing substantial muscle weakness" with a dosage in the claimed range of dosages.

Regarding a method of reducing inflammation comprising administering botulinum toxins B-G, Applicant's arguments that "one of ordinary skill in the art, without any undue experimentation , would be able to treat inflammation using a

dose of botulinum toxin B in LD 50 units that is 50 to 100 times the dose disclosed in the specification as effective for botulinum toxin A," comprises mere assertion and is insufficient to support claims drawn to unpredictable methods of treating neurogenic inflammation further comprising the limitations of interrupting a neurogenic pathway associated with said neurogenic inflammation as set forth in Claim 17.

9. The instant application claims the benefit of priority to Provisional Application No. 60/097,864. Applicant presumably intends to claim priority to Provisional Application No. 60/097,846. Claims 1 and 5-8 are granted said benefit of priority. However, the '846 application does not disclose the use of a chemodenervation agent at doses sufficient to reduce inflammation but insufficient to cause substantial muscle weakness. Neither does the '846 application teach a method for treating neurogenic inflammation. Accordingly, Claims 2-4 and 17-23 are denied the benefit of priority. The priority date of said claims is the filing date of the instant application, 8/25/99.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 3c of this title before the invention thereof by the applicant for patent.

11. Claims 1, 5-6, and 17-23 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,063,768 (filed 9/04/97), for the reasons of record as set forth in Paper No. 11, mailed 7/05/01.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1, 5-8, 10-12, and 17-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No.

6,063,768 (filed 9/04/97)) in view of The Merck Manual (1992) for the reasons of record as set forth in Paper No. 11, mailed 7/05/01.

14. Applicant's request that an interference be declared between the instant application and U.S. Patent No. 6,063,768 is again acknowledged. However, no interference shall be established until such time as all pending claims are found allowable **and** Applicant has submitted appropriate evidence showing entitlement to said declaration. Applicant's understanding regarding "the statutes, rules, and governing sections of the MPEP is that no interference shall be declared until all pending claims are found allowable other than with regard to prior art rejections over the patent with which an interference is sought and applicant has submitted prima facie evidence of prior conception sufficient to show entitlement to a declaration of interference" is correct. At such time as all rejections, other than those over the '768 patent, have been withdrawn, the Examiner will consider whether an interference shall be declared.

15. No claim is allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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January 09, 2002

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